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Non-reductive Conversion of 1-Nitro-9,10-anthraquinone to 1-Amino-9,10-anthraquinones Using Ureas in *N,N,N',N'*-Tetramethylurea (TMU)

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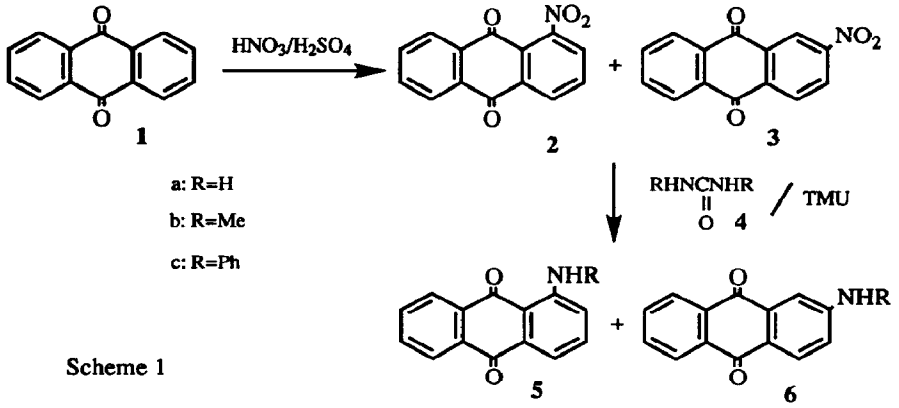
Abstract: Heating 1-nitro-9,10-anthraquinone **2** with ureas **4** in *N,N,N',N'*-tetramethylurea (TMU) at around 130 °C resulted in the displacement of the nitro group by the amino groups, leading to the corresponding aminoanthraquinones **5** in good yields.

1-Amino-9,10-anthraquinone **5a** is widely used for the manufacture of important dyestuffs and pigments.[1,2] Previously, this compound was obtained by the mercury-catalyzed sulfonation of 9,10-anthraquinone **1** with oleum, followed by arsenic-assisted ammonolysis of the resulting sulfonic acid.[1] Over the past two decades another method, based on the nitration of anthraquinone **1** and subsequent reduction of the nitro compound **2** to afford **5a** (Scheme 1), has replaced the classical process mainly because of the pollution problems which the use of toxic element has created.[3] Other minor processes include the acid-catalyzed cyclization of 2-(2-aminobenzoyl)benzoic acid and the arsenic-induced ammonolysis of 1-chloroanthraquinone.[1] One major drawback of the currently ongoing nitroanthraquinone process is the necessity for removal of the accompanying 2-amino isomer **6a** and some diamino derivatives to obtain **5a** in high state of purity, since the conventional reduction methods using alkali sulfides or metal/acid systems do not discriminate the nitro groups at different ring positions.



Scheme 1

The nitro group is commonly employed to activate halogen, alkoxy, alkylthio, sulfonyl and other substituent groups in nucleophilic aromatic substitution, but the displacement of a nitro group itself by nucleophiles is not common process in organic synthesis.[4] In a German patent,[5] compound **2** has been described to undergo aminodenitration when heated with ammonia, urea or ammonium chloride at 135-170 °C in the presence of formamide or *N*-methyl-2-pyrrolidone (NMP). Our attempts to aminate **2** by heating with aqueous ammonia at 130-170 °C for 4-8 h in an autoclave in the presence or absence of a copper catalyst resulted in the formation of expected aminoanthraquinone **5a** accompanied by a considerable amount of tarry substance. The reaction of **2** with urea in NMP under the similar conditions led to a complex mixture of **5a** and several other unidentified products. However, we have found that heating of nitroanthraquinone **2** with excess of urea in *N,N,N',N'*-tetramethylurea (TMU)[6] at around 130 °C can lead to **5a** in good yield.

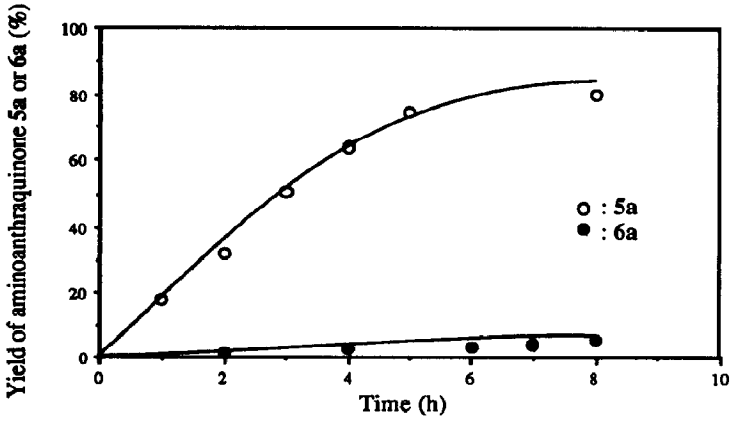


Fig. 1 Profiles for the reaction of nitroanthraquinones **2** and **3** with urea **4a** in TMU at 130 °C. The substrate-reagent ratio was 1:16.

Because of its rigid hydrogen bond network, urea **4a** is only slightly soluble in non-hydroxylic organic solvents, but it readily dissolves in hot TMU. When compound **2** was gently heated with a large excess of urea in TMU at around 130 °C, the nitro group was gradually displaced by the amino group to give **5a** in good yield (Table 1). A typical procedure for the amination is as follows: A mixture of **2** (0.20 g, 0.79 mmol), urea **4a** (3.0 g, 50 mmol) and TMU (3.1 mL) was heated with stirring at around 130 °C for 8 h. After cooling the mixture was diluted with saturated aqueous sodium hydrogen carbonate (40 mL) and the organic phase was extracted with benzene. The solvent was evaporated and an oily residue was gently heated under reduced pressure to recover TMU to the last drop. Recrystallization of the dry powdery solid from ethanol gave **5a** (purity >95 %) as orange-red needles, yield, 0.164 g (93 %).

The nitro group at 1-position is more reactive than the one at 2-position (Fig. 1). Thus, when an equimolar mixture of nitroanthraquinones **2** and **3** was subjected to the present reaction and worked up at *ca.* 70% conversion stage, the ratio of aminoanthraquinones **5a** and **6a** was *ca.* 20:1, the former isomer being enriched considerably in the product. Among several dipolar aprotic solvents examined, TMU gave the most

Table 1 Amination of 1-nitro-9,10-anthraquinone **2** with ureas **4a-c** in TMU[a]

Run	Substrate	Urea **4** (equiv)	Reaction time (h)	Conversion[b] (%)	Yield[c] (%)
1	1-Nitro-9,10-anthraquinone (1-NO_2AQ) R=H	16	9	86	73
2	1-NO_2AQ	32	8	92	83
3	1-NO_2AQ	64	8	98	93
4	2-Nitro-9,10-anthraquinone (2-NO_2AQ)	16	9	30	5
5	1-NO_2AQ + 2-NO_2AQ (1:1)	16	11	70 + 7 (**5a**:**6a**=10:1)	62 + 3 (**5a**:**6a**=21:1)
	R=Me				
6	1-NO_2AQ	32	25	88	83
	R=Ph				
7	1-NO_2AQ	12	48	—[d]	46

[a] All reactions were carried out using the given substrate (0.8 mmol) and TMU (3 mL) at 130 °C, unless otherwise indicated. Purity of nitroanthraquinones used was 99%.

[b] Conversion was determined at column temperature 40 °C on a Shimadzu FRC-10A liquid chromatograph equipped with an Inertsil ODS-2 column (GL Science Co. Ltd.) using MeCN-H_2O (1:1) as an eluent. Naphthalene was used as an internal standard.

[c] Yields refer to the isolated compouds (purity >95%) and were not optimized. Impurity was unchanged substrate.

[d] Not determined.

satisfactory results. It proved to be the best solvent system to obtain a high concentration of urea in solution. NMP and *N,N'*-dimethylimidazolidone gave acceptable results also, but hexamethylphosphoric triamide and *N,N*-dimethylformamide were unsuitable as a solvent, since they were found to behave as the aminating agent for the nitroanthraquinones. Direct fusion of nitroanthraquinone **2** with an excess of urea **4a** proved to be disappointing, because the product was always accompanied by a considerable amount of polymeric matter derived from urea, especially when the conversion of **2** was brought to near completion. In contrast, the reaction run in TMU led to **5a** free from side products; only after prolonged heating at higher temperatures (>135 °C), the product was accompanied by small amounts of 1-(*N*-methylamino)-9,10-anthraquinone **5b** and some decomposition products from urea, which could be easily removed through aqueous work-up and subsequent recrystallization from ethanol.

When urea **4a** was replaced by *N,N'*-dimethylurea **4b**, the product was **5b**. Similarly, the use of *N,N'*-diphenylurea **4c** as the aminating agent gave 1-(*N*-phenylamino)-9,10-anthraquinone **5c** as a sole product, although the reaction was quite slow. Being an extremely weak base, aminoanthraquinone **5a** is usually *N*-alkylated by heating it with an alcohol or a dialkyl sulfate in concentrated sulfuric acid at 180-200 °C. Arylation of **5a** is accomplished by heating it with an aryl bromide at high temperatures in the presence of copper powder or a copper salt.

The present amination method is highly *regio-specific*. Of three isomeric dinitrobenzenes subjected to the reaction at around 110 °C, only 1,2-dinitrobenzene underwent facile amination to yield 2-nitroaniline, whereas the other two isomers were recovered almost quantitatively. Upon similar treatment, 3,4-dinitrotoluene and 3,4-dinitrochlorobenzene underwent preferential displacement of a nitro group at 3-position, giving 5-methyl-2-nitroaniline and 2-nitro-5-chloroaniline as the respective products. Second amination did not take place. Further details on the scope and limitations of this interesting methodology will be reported elsewhere in due course.

Acknowledgment

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